

## **REMARKS**

### **A. Status of the Claims**

Claims 1-6 were examined in the Office Action mailed January 4, 2007. Claims 7-12 stand withdrawn. Claims 1-2 are presently canceled. Claim 3 has been written into independent form, and new claims 13-19 have been added. Support for new claims 13-19 may be found in the specification and examples, at least at paragraphs 8, 9, 10, and 11. Claims 3-6 and 13-19 are currently pending.

### **B. The Pending Claims Are Nonobvious Over the Prior Art**

The Action rejected claims 3, 5, and 6 under 35 U.S.C. § 103(a) as unpatentable over U.S. Pat. No. 4,505,896 to Bernstein (“Bernstein”). Claim 4 was rejected as obvious over Bernstein, in view of U.S. Pat. No. 6,248,763 to Scivoletto (“Scivoletto”). Finally, all of the claims were rejected as obvious over U.S. Pat. No. 6,429,218 to Scivoletto et al. (“Scivoletto II.”). The Action’s rejection of the claims is improper because of errors in the way the action applies the legal analysis of obviousness as set forth in *Graham v. John Deere*, and further for failing to consider the objective indicia of nonobviousness present in the specification.

In particular, the Action fails to fully consider the objective indicia of nonobviousness present in the specification that include evidence of unexpected, synergistic results. The application itself specifically states that the disclosed compositions provided surprising results over the prior art—that the addition of a small amount of nicotinic acid to standard amounts of nicotinamide resulted in a far superior acne treatment that could not have been predicted based on the prior use of the active ingredients separately. Furthermore, the application also provides working examples which demonstrate this dramatically improved efficacy of the claimed compositions relative to the prior art. Indeed, in one example, the currently claimed composition

entirely cleared a patient's face of acne lesions, even though patient had been non-responsive to a prior art, nicotinamide-only composition. Application, at ¶ 11.

There is little indication that the Communication genuinely considered the *John Deere* factors in making the improper rejections over Bernstein, Scivoletto, and Scivoletto II. As set forth in MPEP 2141, consideration of these factors is required by the Office, specifically to prevent the kind of hindsight reconstruction that the Action employs in making this improper rejection. Applicant sets forth an analysis of the *John Deere* factors below, including evidence of secondary considerations, to demonstrate that the claimed invention is nonobvious over Bernstein, Scivoletto, and Scivoletto II.

### **1. Determining the scope and content of the prior art**

With respect to the claimed invention, none of the three prior art references cited by the examiner teach all of the limitations of the pending claims.

**The Bernstein reference does not suggest the combination of nicotinamide and nicotinic acid as erroneously stated in the Action.**

The Action fails in its analysis of the scope and content of the Bernstein reference. Bernstein does not teach or suggest the combination of nicotinic acid with nicotinamide for the treatment of acne vulgaris or rosacea as erroneously stated in the Action. Instead, Bernstein specifically teaches the use of nicotinamide or nicotinic acid as interchangeable alternatives in oral or topical administration forms. For example, Bernstein describes compositions comprising “an effective amount of nicotinic acid or nicotinamide or combination thereof with sulfur, salicylic acid” etc.—meaning that either nicotinic acid or nicotinamide might be used alone or either nicotinic acid or nicotinamide might be used in combination with other acne treatments. Bernstein, at col. 1, lns 65-66. Similarly, Bernstein later recites:

The present invention includes within the scope thereof pharmaceutical compositions suitable for both topical and oral administration having as an active

ingredient thereof nicotinic acid or nicotinamide. Also included in the scope of the invention is the combination of nicotinic acid or nicotinamide with one or more of sulfur, salicylic acid . . . .

Bernstein, at col. 5, lns 4-10 (emphasis added). Thus, Bernstein consistently describes nicotinic acid and nicotinamide as alternatives that might be used interchangeably. This is reinforced by the fact that in the 16 examples provided in the Bernstein specification, **none** of them teach a combination of nicotinamide with nicotinic acid, while many of them do teach the interchangeable use of nicotinamide or nicotinic acid. Bernstein, at cols. 2-5.

Bernstein, therefore, in no way teaches or suggests the combination of nicotinamide and nicotinic acid and in no way suggests that the addition of a small amount of nicotinic acid to a composition of nicotinamide would be beneficial in a method of treating acne as in the rejected claims. Applicant respectfully asserts, therefore, that all rejections over Bernstein should be withdrawn.

**The Scivoletto reference does not cure the deficiencies of Bernstein, because Scivoletto does not teach or suggest the combination of nicotinamide and nicotinic acid that is also missing from Bernstein.**

Scivoletto describes topical compositions for the treatment of acne, as well as compositions to be used as daily face cleansers, lipsticks, and makeup. With respect to compositions for acne treatment, the Scivoletto specification provides a composition comprising methyl nicotinate in an amount of 0.01 to 1% and niacin in an amount of 0.01 to 1%. Scivoletto, at col. 2, lns 55-56. However, the specification also states that “the active ingredient listed is methyl nicotinate” and that “nicotinamides, derivatives thereof, nicotinic acids, nicotinic esters or derivatives thereof” might also be substituted for methyl nicotinate as the active ingredient in the composition. Scivoletto, at col. 2, lns 45-49. Thus, Scivoletto teaches a genus of compositions including “nicotinamides” or “nicotinic acids” as the active ingredient at a concentration of 0.01

to 1% and, further comprising niacin at a concentration of 0.01 to 1%. Accordingly, Scivoletto teaches an amount of nicotinamide that, at best, is ½ the amount required by the pending claims.

Scivoletto, however, in no way describes or suggests the use of a composition that includes 2-10% nicotinamide, and neither does Scivoletto suggest a combination of nicotinamide and nicotinic acid as in the rejected claims, nor that such a combination would provide the surprising results shown in Applicant's specification. This rejection over Bernstein in view of Scivoletto, therefore, should be withdrawn.

**Scivoletto II does not describe any method of treating acne vulgaris or acne rosacea as in the pending claims, nor does Scivoletto II suggest a method of treating acne with a combination of nicotinic acid and nicotinamide as in the pending claims.**

Scivoletto II describes a “face cream for extra oily skin” comprising methyl nicotinate at a concentration of 0.01 to 2.5% and nicotinic acid at a concentration of 0.01 to 2.5%. Scivoletto II, at col. 3, lns 24-25. Scivoletto II also describes an additive, used for increasing the **active ingredient** concentration in a base cream, comprising “0.01% to 3% of nicotinic acid (niacin) and esters, and amides at 0.01% to 20%.” Scivoletto II, at col. 3, ln 39 – col. 4, ln. 10.

It appears that the Action again misinterprets the prior art. The plain language of Scivoletto II only suggests that one can increase the strength of the base formula, by adding an additional amount of the active ingredient that is in the base formula, i.e., one can add nicotinic acid to a base formula that contains nicotinic acid Scivoletto II, at col. 3, line 36- col. 4, line 11. Nowhere does Scivoletto suggest adding a different ingredient to the base formula.

**Because the claimed method of treating acne with the claimed combination of nicotinamide and nicotinic acid yields benefits that could not be predicted from the use of the same amounts of the active ingredients alone, the claims cannot be obvious.**

The recent Supreme Court decision, *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) provides further instruction on the use of the analysis set forth in *Graham*. In providing guidance for the application of *Graham*, the Court relied on the principle that a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results, but that when elements work together in an unexpected and fruitful manner, then those combinations are not obvious.

First, Bernstein consistently describes nicotinamide and nicotinic acid as interchangeable alternatives. Given the similar chemical structures of nicotinamide and nicotinic acid and the apparently interchangeability of the two from Bernstein, there would have been no suggestion that two interchangeable ingredients would be more useful in the same composition, particularly in the specific concentration ranges claimed.

Second, although Scivoletto does provide an acne treating composition including 0.01 to 1% niacin, Scivoletto does not suggest that the addition of such a concentration of niacin to a nicotinamide formulation would provide synergistic positive results in the treatment of acne as shown in Applicant's examples.

Finally, the cited compositions in Scivoletto II are directed towards a “face cream for extra oily skin” and an “added strength ampoule” used to “increase the strength of the active ingredient little by little.” Scivoletto II, at col 3, ln 23; col. 4, lns 6-7. Thus Scivoletto II only suggests increasing the strength of the active ingredient already contained in the base formulation, and not combining active ingredients in order to achieve a synergistic effect. Additionally, these compositions are not described for the treatment of acne vulgaris or acne rosacea.

In sum, none of the prior art teaches the compositions used in the methods of the pending claims. Additionally, the combination of the cited references in no way suggests that the methods utilizing the claimed combination of ingredients would have the beneficial effects as shown in

Applicant's examples. The scope and content of the prior art, therefore does not include, nor suggest the claimed inventions.

**2. Differences between Bernstein, Scivoletto, and Scivoletto II and the claimed inventions.**

As amended, claim 3 recites:

3. A method of treating acne vulgaris and acne rosacea comprising applying to the skin of patients afflicted with such disorders a topical composition comprises about 2-10% nicotinamide by weight combined with about .005-.7% nicotinic acid by weight.

The remaining pending claims depend from claim 3, and thus, all of the claimed methods require a topical composition comprising both nicotinamide and nicotinic acid as set out in claim 3.

None of the prior art references alone describe a composition for treating acne vulgaris and acne rosacea comprising both nicotinamide at a concentration of 2-10% and nicotinic acid at a concentration of .005 to 0.7%. As discussed above, Bernstein does not contemplate the simultaneous or combined use of nicotinamide and nicotinic acid. Scivoletto teaches a genus of compositions including “nicotinamides” or “nicotinic acids” as the active ingredient combined with niacin, the concentration ranges provided for the genus of active ingredient “nicotinamides”—0.01 to 1%—does not fall within, or even overlap the claimed range of 2 to 10% for nicotinamide in the application, and Scivoletto II does describe methods for the treatment of acne vulgaris or acne rosacea, but rather the cited compositions are directed towards a “face cream for extra oily skin” and an “added strength ampoule” used to “increase the strength of the active ingredient little by little.” Scivoletto II, at col 3, ln 23; col. 4, lns 7-8. Consequently, the cited references, either alone or in combination do not teach or suggest a method of treating acne vulgaris or acne rosacea with a topical composition comprising an amount of about 2-10%

nicotinamide by weight and about .005-0.7% nicotinic acid by weight. Neither do the cited references suggest the surprising benefits of such methods.

### **3. The level of skill in the pertinent art**

The level of skill in the pertinent art would be a person with several years of experience in formulating pharmaceuticals. The purpose of the level of skill determination is to determine what is inherently disclosed in the prior art, or what a person would know when faced with the problem addressed by the invention. In the present case, a reading of Bernstein, Scivoletto, and Scivoletto II and the array of formulations provided in those references, would not have led one of ordinary skill in the art to combine small amounts of nicotinic acid with nicotinamide as was done by the Applicant.

### **4. Evidence of objective considerations**

Examples of objective evidence that tend to show non-obviousness include copying, commercial success, industry acclaim and recognition, long-felt need, failure of others, and licensing by industry. Objective evidence must be considered in every case in which they are present. See MPEP §2141. Moreover, “[e]xaminers must consider comparative data in the specification which is intended to illustrate the claimed invention in reaching a conclusion with regard to the obviousness of the claims. *In re Margolis*, 785 F.2d 1029, 228 USPQ 940 (Fed. Cir. 1986).” MPEP § 716.01(a).

In this case, the Action ignored such evidence of surprising and unexpected results present in the application, specifically, the surprising and unexpected synergy seen from the combination of a small amount of nicotinic acid with nicotinamide. Directly on this point, the application states:

In searching for a method to increase the efficacy of topical nicotinamide, I discovered surprisingly, that by adding a very small amount of nicotinic acid to topical formulations of nicotinamide, the resulting product was far more effective

at treating acne vulgaris or acne rosacea than were formulations containing nicotinamide alone.

Application, at ¶ 5. Moreover, the application objectively substantiates these claims with comparative data demonstrating that the formulation claimed in the instant application provides surprising results over the prior art:

A 29 year-old female with acne vulgaris and more than 10 inflammatory acne papules or pustules applied an emulsion containing 4% nicotinamide and 0.05% nicotinic acid. Although she had used a similar emulsion containing 4% nicotinamide without the nicotinic acid, **and had not been responsive to it**, with the new emulsion containing both nicotinamide and nicotinic acid the patient's acne lesions **cleared completely** after four weeks of once daily treatment.

Application, at ¶ 11 (emphasis added).

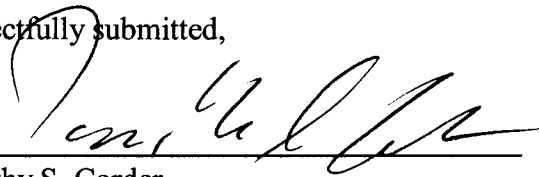
The dramatically improved effectiveness of the instant claimed compositions over the prior art is also evident from the relative descriptions of the effectiveness of the Applicant's compositions and those of the prior art. For example, in Bernstein, the prior art topical formulations were described to provide only "a noticeable decrease in the inflammatory lesions," Bernstein, at col. 3, lns. 10-11. Similarly, Scivoletto reports "improved . . . acne condition" with its compositions. Scivoletto, at col. 3, lns. 36-37.

In contrast, in the instant application, treatment according to the claimed method renders subjects' faces "clear of any inflammatory acne lesions" or "totally normal and free of rosacea lesions." Application, at ¶ 9-10. Thus, the claimed compositions and methods result in significantly improved outcomes for the treatment of acne vulgaris and acne rosacea relative to the prior art. The surprising and unexpected synergy resulting from the addition of a small amount of nicotinic acid to nicotinamide is strong, objective evidence of nonobviousness.

### CONCLUSION

Applicant respectfully submits that, in light of the preceding discussion and amendments, the present claims are in condition for allowance, and further respectfully requests that all rejections over Bernstein, Scivoletto, and Scivoletto II, be withdrawn. If the Examiner has any questions or suggestions that might expedite the allowance of the pending claims, a telephone call to the undersigned representative at 512.542.8446 would be welcomed.

Respectfully submitted,



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